

Amendments to the Claims

I. Amendments

Please cancel claims 1-2, and 4-46, without prejudice or disclaimer thereto.

Please amend claim 3 as indicated below, and add new claims 47-65.

II. The Claims of the Application

Claims 1.-2. **(Cancelled)**

Claim 3. **(Currently Amended)** A method of producing a composition containing The modified protein or polypeptide molecules, or salts thereof, wherein said modified protein or polypeptide molecules of said composition consist essentially of a compound selected from of claim 1 having the formula



in which



wherein

A is a residue of a protein or polypeptide having a carboxy and amino terminus and is connected to X-Z-X'-B exclusively at said carboxy or amino terminus;

B is a polymeric compound residue of a protein or polypeptide, a reporter group or a cytotoxic agent;

X and X' independently from each other are bivalent organic radicals or independently from each other are present or may be absent;

In Re New Continuation Application of
 U.S. Patent Appln. Serial No: 08/241,687
 Inventors: Offord, R.E. *et al.*

Z is a bivalent radical selected from the group consisting of:
 -C(R)=N-, -N=C(R)-, -CH(R)-NH-, -NH-CH(R)-,
 -C(R)=N-Y-N=C(R)-, -N=C(R)-Y-C(R)=N-,
 -CH(R)-NH-Y-NH-CH(R)- and -NH-CH(R)-Y-CH(R)-NH-,
-C(R)=N-O- , -O-N=C(R)- , -CH(R)-NH-O- , -O-NH-CH(R)- ,
-C(R)=N-O-Y-O-N=C(R)- , -O-N=C(R)-Y-C(R)=N-O- ,
-CH(R)-NH-O-Y-O-NH-CH(R)- and -O-NH-CH(R)-Y-CH(R)-
NH-O- ;

where

R is hydrogen or an aliphatic, cycloaliphatic, aromatic or
 araliphatic hydrocarbon group, ~~which group may be substituted
 with the same or a different protein or polypeptide, a reporter
 group or a cytotoxic agent, with at least one aromatic radical or
 oxygen adjacent to nitrogen;~~ and

Y is a bivalent organic group,

wherein said method comprises condensing a compound of the
 formula:

A-X-R¹

wherein R¹ is a -CO-R group, an acetalized formyl group, or an
 amino or protected amino group, and A, R, and X are as defined
 above, with a compound of formula:

R²-X'-B

or a compound of formula:

R²-Y-R²

where R² is amino when R¹ is -CO-R or acetalized formyl and R² is -
 CO-R or acetalized formyl when R¹ is amino, and X', Y, R and B are
 as defined above, to form a Schiff base, hydrazone, oxime or
 azomethine compound, and optionally,

reducing the $-C(R)=N-$ or $-N=C(R)$ formed by the condensation to
 $CH(R)-NH-$ or $-NH-CH(R)-$, respectively, and optionally forming a
salt.

Claims 4-46 (Cancelled)

Claim 47. (New) The method of producing a composition of claim 3, wherein said residue A is a carboxy terminal residue.

Claim 48. (New) The method of producing a composition of claim 3, wherein said residue A is an amino terminal residue.

Claim 49. (New) The method of producing a composition of claim 3, wherein said polymeric compound B is a protein or polypeptide that is the same or different from said protein or polypeptide A, or is a reporter group or cytotoxic agent.

Claim 50. (New) The method of producing a composition of claim 49, wherein said polymeric compound B is a protein or polypeptide that is the same as said protein or polypeptide A.

Claim 51. (New) The method of producing a composition of claim 49, wherein said polymeric compound B is a protein or polypeptide that is different from said protein or polypeptide A.

Claim 52. (New) The method of producing a composition of claim 49, wherein said polymeric compound B is a reporter group.

Claim 53. (New) The method of producing a composition of claim 49, wherein said polymeric compound B is a cytotoxic agent.

In Re New Continuation Application of
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Claim 54. (New) The method of producing a composition of claim 52, wherein said polymeric compound B is a reporter group comprising a metal chelating organic compound.

Claim 55. (New) The method of producing a composition of claim 3, wherein R is hydrogen.

Claim 56. (New) The method of producing a composition of claim 3, wherein said polymeric compound B comprises a compound selected from the group consisting of:

- (i) desferrioxamine B, or a metal derivative thereof;
- (ii) diethylenetriaminepentaacetic acid, or a metal derivative thereof;
- (iii) $[\text{N}\varepsilon\text{-(diethylenetriaminepentaacetic acid -alanyl)-Lys}]_5$, or a metal derivative thereof; and
- (iv) a polyglutamic acid having at least two ferioxamine B residues coupled thereto.

Claim 57. (New) The method of producing a composition of claim 3, wherein Z is $-\text{CH}_2\text{-NH-}$, or $-\text{NH-CH}_2-$.

Claim 58. (New) The method of producing a composition of claim 3, wherein Z is $-\text{C}(\text{R})=\text{N-}$, or $-\text{N}=\text{C}(\text{R})-$.

Claim 59. (New) The method of producing a composition of claim 3, wherein Z is $-\text{CH}(\text{R})\text{-NH-}$, or $-\text{NH-CH}(\text{R})-$.

Claim 60. (New) The method of producing a composition of claim 3, wherein Z is $-\text{C}(\text{R})=\text{N-O-}$ or $-\text{O-N}=\text{C}(\text{R})-$.

In Re New Continuation Application of
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Claim 61. **(New)** The method of producing a composition of claim 3, wherein Z is
CH(R)-NH-O-, -O-NH-CH(R)- .

Claim 62. **(New)** The composition of claim 3, wherein Z is
-C(R)=N-Y-N=C(R)-, -N=C(R)-Y-C(R)=N-, -CH(R)-NH-Y-NH-CH(R)-
or -NH-CH(R)-Y-CH(R)-NH-.

Claim 63. **(New)** The composition of claim 3, wherein Z is
-CH=N-Y-N=CH- , -N=CH-Y-CH=N- , -CH₂-N-Y-N-CH₂- ,
or -NH-CH₂-Y-CH₂-NH- .

Claim 64. **(New)** The composition of claim 3, wherein Z is
-C(R)=N-O-Y-O-N=C(R)- , -O-N=C(R)-Y-C(R)=N-O-.

Claim 65. **(New)** The composition of claim 3, wherein Z is
-CH(R)-NH-O-Y-O-NH-CH(R)- or
-O-NH-CH(R)-Y-CH(R)-NH-O-.